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THE FORMATION OF SCHIFF BASE FROM DIMETHYL α , β-DIBROMOSUCCINATE AND AN ASYMMETRIC SYNTHESIS OF ASPARTIC ACID*

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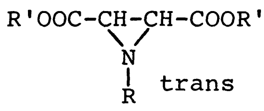
The reaction of α-methylbenzylamine with dimethyl meso and racemic dibromosuccinate resulted in the formation of trans-aziridine(Ib) and Schiff base(III) of dimethyl oxaloacetate. The optically active III was hydrogenated and hydrogenolyzed to form optically active aspartic acid(V). The optical purity of V reached up to 49 %.

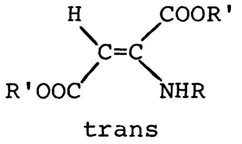
Stereochemical studies on the reaction of ammonia with diethyl meso and racemic α , β-dibromosuccinate, diethyl α-bromofumarate and diethyl α-bromomaleate have been reported.[1)] Each of these reactions gave two products, trans-aziridine(Ia) and trans-enamine(IIa).

In the present paper, we have investigated the reaction of racemic α-methylbenzylamine with dimethyl meso and racemic dibromosuccinate. The reactions were carried out at room temperature using ethyl alcohol as the solvent. Two same compounds were isolated by silica gel column chromatography in each reaction. The first compound was confirmed as trans-aziridine(Ib)(yield 33~35 %) by the chemical behavior and the IR and NMR analyses.[2)] However, the second compound was not enamine (II) as was expected by the literature,[1)] but isomeric Schiff base(III)(yield 54~57 %) of dimethyl oxaloacetate with racemic α-methylbenzylamine. The expected enamine(IIb) was not isolated from the reaction mixture. The Schiff base(III) was an oily material and it did not crystallize. The structure of III was confirmed by IR and NMR analyses.[3)]



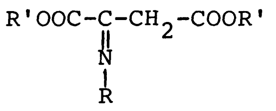
Ia R : H, R': C_2H_5

Ib R : $-CH(CH_3)-C_6H_5$
R': $-CH_3$



IIa R : H, R': C_2H_5

IIb R : $-CH(CH_3)-C_6H_5$ R(+) S(-)
R': $-CH_3$



$R'OOC-C(=N-R)-CH_2-COOR'$

III R : $-CH(CH_3)-C_6H_5$ R(+) S(-)
R': $-CH_3$

The optically active III was prepared from R-(+)- and S-(-)-α-methylbenzylamine and dimethyl meso-dibromosuccinate in a similar way. The III was hydrogenated by

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* Sterically Controlled Syntheses of Optically Active Organic Compounds. XXII. Part XXI: Bull. Chem. Soc. Jpn., 46, 1901 (1973).

the use of palladium on charcoal and then hydrolyzed with 6N hydrochloric acid.$^{4)}$ The resulting N-alkyl aspartic acid(IV) was hydrogenolyzed by the use of palladium hydroxide on charcoal to form optically active aspartic acid(V).$^{5)}$ The chiral V was isolated by the use of Dowex 50 column(H^+ form) by eluting with aqueous ammonia. The summerized results of the asymmetric synthesis of V are shown in Table 1. The yield of V was in a range of 43 to 56 % and the optical purity of V reached up to 49 % when methanol was used as the solvent. The use of R(+)-α-methylbenzylamine resulted in the formation of R-aspartic acid. The optical purity of V decreased steadily by the use of alcohols having larger alkyl groups(lower dielectric constants) and the configuration of V was inverted by the use of t-butyl alcohol.

Table 1 Optically active aspartic acid from Schiff bases by reductive amination

exp$^{a)}$	amine$^{b)}$	solvent	config.of V	$[\alpha]_D^{25}$(5NHCl)	e.e.$^{c)}$ %	synthetic$^{d)}$ yield %
1	DL	MeOH	-	-	-	51
2	R(+)	MeOH	R	-12.5(c=1.16)	49	56
3	R(+)	EtOH	R	- 8.5(c=1.26)	33	50
4	R(+)	n-PrOH	R	- 3.1(c=1.65)	12	48
5	R(+)	i-PrOH	R	- 0.7(c=1.88)	3	52
6	R(+)	t-BuOH	S	+ 1.3(c=1.12)	5	56
7	S(-)	n-PrOH	S	+ 2.7(c=1.66)	11	43
8	S(-)	t-BuOH	R	- 1.9(c=1.10)	8	47

a) optical rotation of Schiff base R(+):$[\alpha]_D^{25}$+57.9°(c=1.92, benzene), S(-):$[\alpha]_D^{25}$-59.5°(c=1.16, benzene).

b) R(+):R(+)-α-methylbenzylamine, $[\alpha]_D^{25}$+39.0° neat; S(-):S(-)-α-methylbenzylamine, $[\alpha]_D^{25}$-39.0° neat.

c) based on the maximum rotation, ±25.4°(c=10.0, 5N HCl).

d) based on the Schiff base.

References and Note

1) K. D. Berlin, L. G. Williams, O. C. Dermer, Tetrahedron Lett., 1968, 873.

2) [Ib]:δ($CDCl_3$) 1.50(3H,d, $-CH-C\underline{H}_3$), 2.50(2H,q,J=6.2Hz, ring proton) 2.77(1H,q, $-C\underline{H}-CH_3$), 3.65(3H,s, $-CO_2C\underline{H}_3$), 3.73(3H,s, $-CO_2C\underline{H}_3$), 7.12-7.50 (5H,m,Ar$\underline{H}$).

3) [III]:δ($CDCl_3$) 1.26-1.52(3H,d,d, J=7.1Hz, syn and anti $CH-C\underline{H}_3$), 3.00(2H,s, $-C\underline{H}_2-$), 3.60(3H,s, $-CO_2C\underline{H}_3$), 3.71(3H,s, $-CO_2C\underline{H}_3$) 3.54-4.18(1H, broad q,$-C\underline{H}-CH_3$), 7.02-7.49(5H,m,Ar$\underline{H}$).

4) R. G. Hiskey and R. C. Northrop, J. Am. Chem. Soc., 83, 4798 (1961).

5) The hydrogenation and subsequent hydrogenolysis of the Schiff base of oxalacetic acid with optically active α-methylbenzylamine do not give aspartic acid but alanine. K. Matsumoto and K. Harada, J. Org. Chem., 33, 4526 (1968).

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